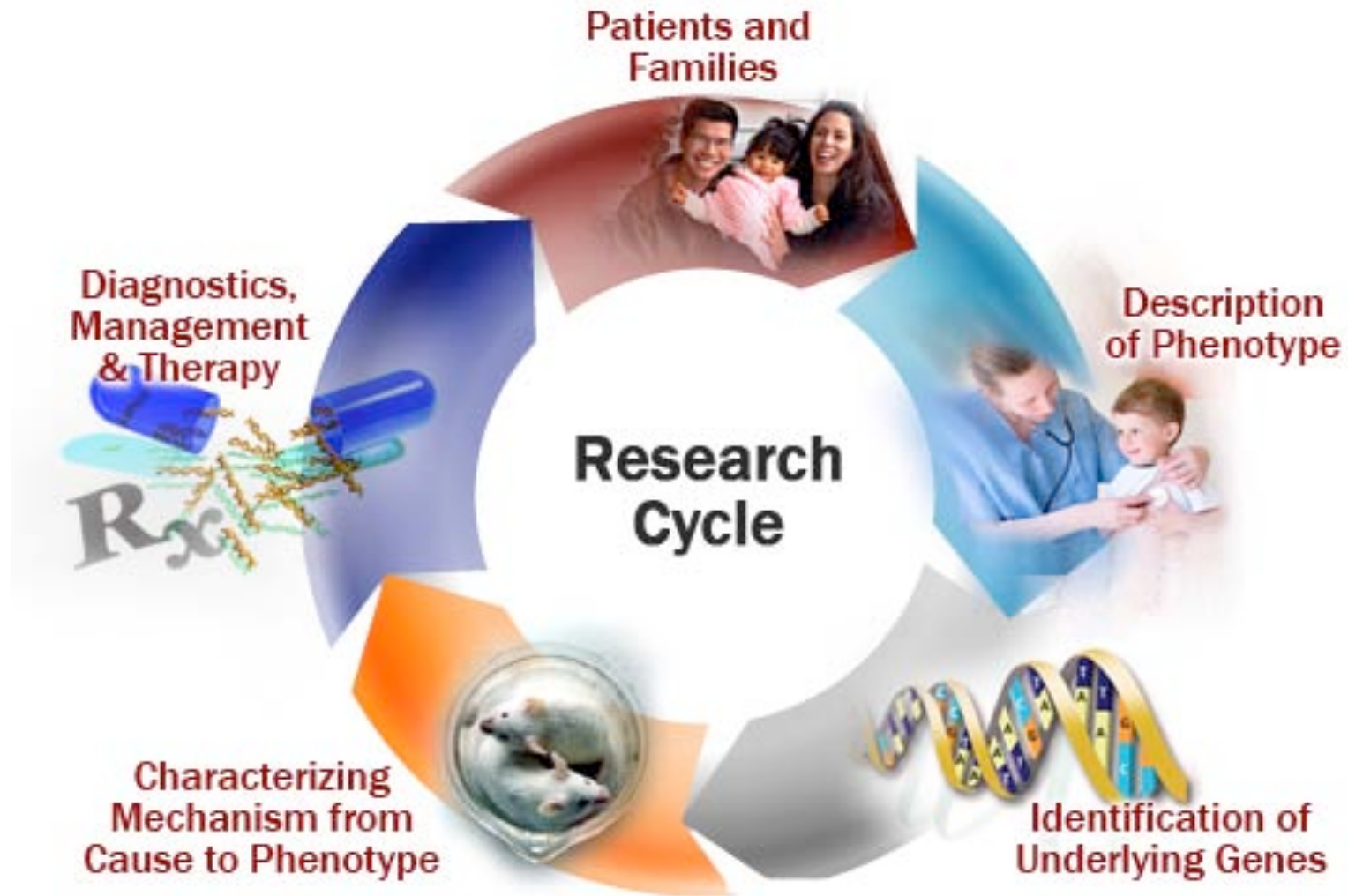


HDSA RESEARCH PARTNERSHIP



Pathogenesis and clinical disease

**HD CAG
Trigger
POLYQ-
HUNTINGTIN**

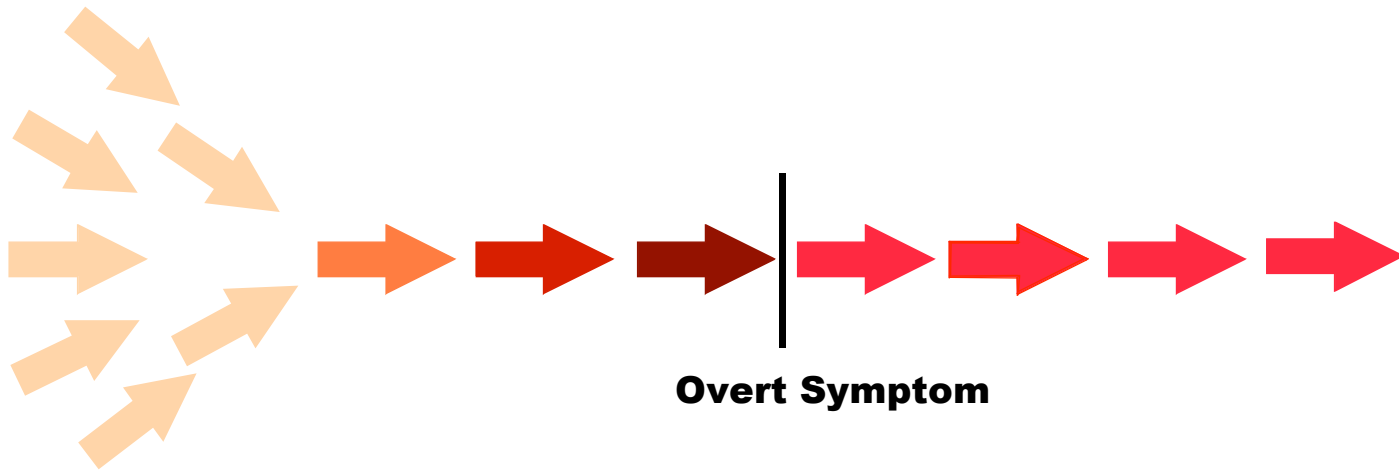


Overt Symptom

Steps in the Presymptomatic Disease Process

Steps in Disease Progression

**Factors
contributing to
disease
susceptibility**



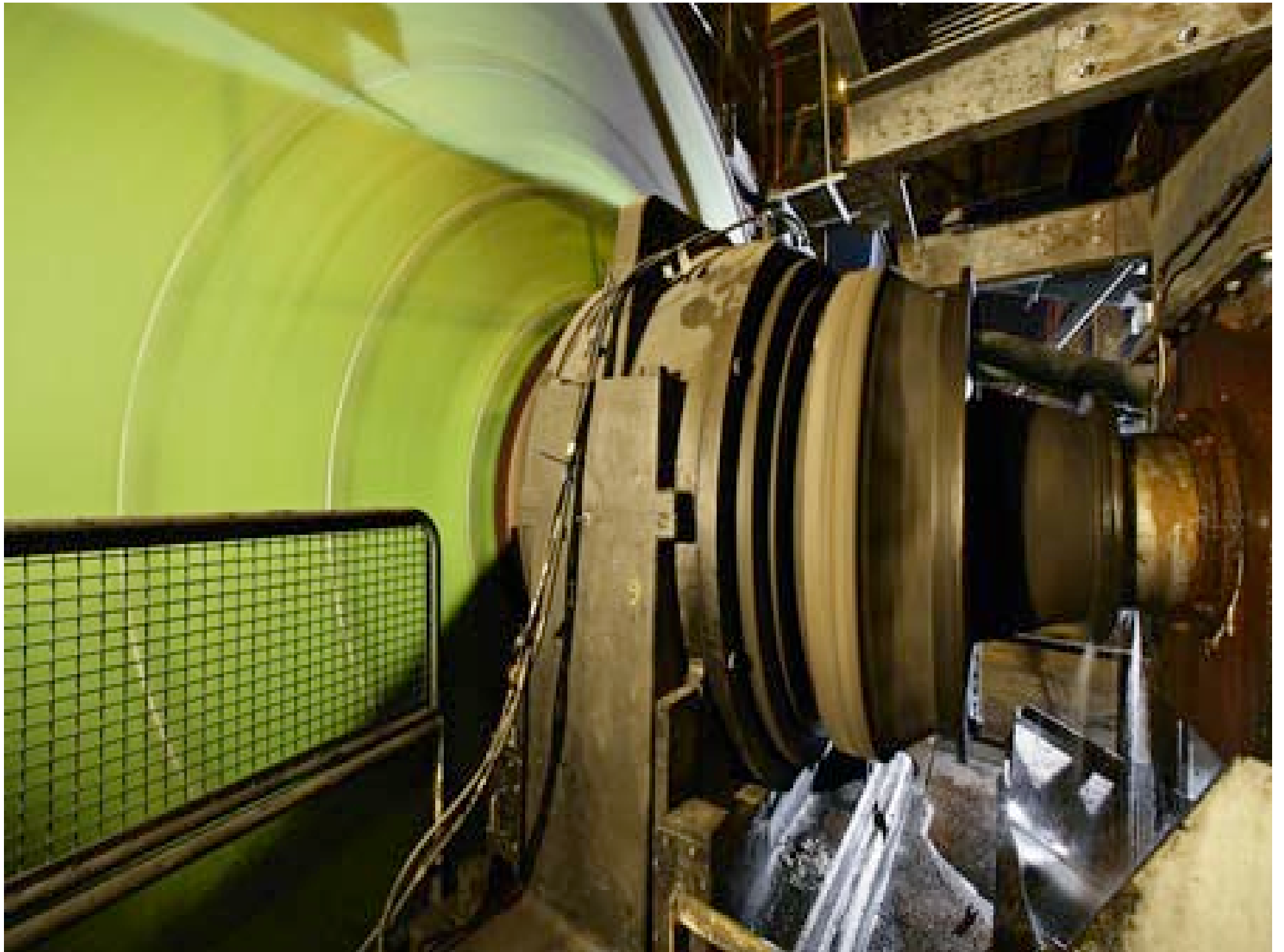
Overt Symptom

Steps in the Presymptomatic Disease Process

Steps in Disease Progression







gettyimages[®]





HDSA Research Pipeline to Treatments

Discovery Research

**Flexibility
variety of
strategies**



Target

**Change
due to the
HD gene**

Applied Research

**Identify
possible
treatment**



**Optimize
possible
treatment**



**Preclinical
testing-
'model
systems'**



Clinical Trial Research

**Phase 1
Clinical
Trial**



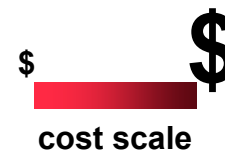
**Phase 2
Clinical
Trial**



**Phase 3
Clinical
Trial**



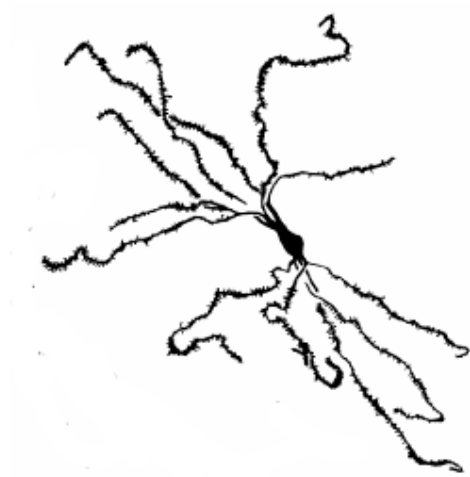
**FDA
approved
drug**



Discovery
Start with the right ore

Grants and Fellowships
Coalition





**Mutant
huntingtin**



Death

Lifeline of a brain cell with the HD mutation

**Trigger
mechanism**

**Changes that disable
the brain cell**

**Changes that kill
the brain cell**

Focus of HDSA Research

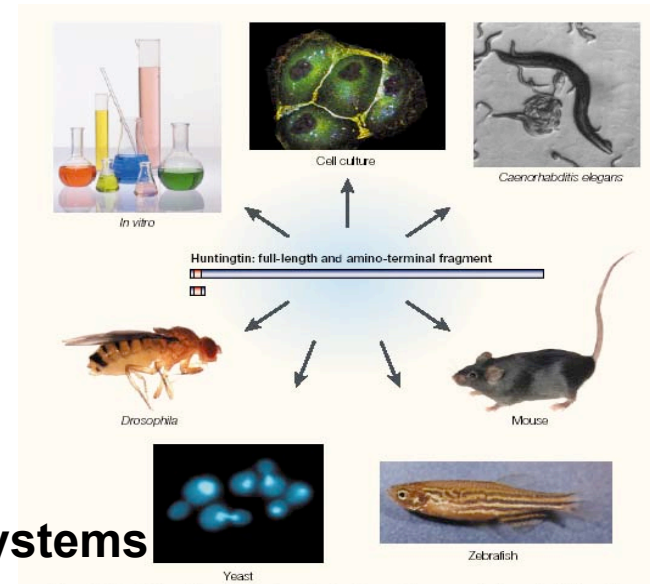
Grants and Fellowships

NEW IDEAS, NEW (DEDICATED) HD RESEARCHERS

- **Vital flexible funding to seed new HD research areas and to support young researchers at the start of their careers**
- **Grant \$50,000 for one year**
- **Fellowship \$40,000 per year (2 years)**



Huntingtin protein



Model systems

Grant Recipient



Dr. Ruth Luthi-Carter, Ph.D.
Swiss Federal Institute of Technology
Lausanne Switzerland
Molecular changes in human HD brain

Fellowship Recipients



Dr. Browen Martin, Ph.D.
National Institutes of Health (Bethesda MD)
Molecules that respond to sugar



Dr. Jean Savare, Ph.D.
J. David Gladstone Institutes (San Francisco CA)
Finding all huntingtin partners in yeast



Dr. Austin Milnerwood, Ph.D. (with HSC)
University British Columbia
Brain cell function in YAC128 HD gene mice

Coalition

16 expert international laboratories committed to cooperative HD research, self-organized into teams aimed at pressing issues in HD research, closely aligned with HSC, CHDI, NIH in order to capitalize quickly on the research findings.

Gillian Bates, Ph.D.

Flint Beal, M.D.

David Borchelt, Ph.D.

Elena Cattaneo, Ph.D.

Jang-Ho Cha, M.D., Ph.D.

Marian Difiglia, Ph.D.

Robert Freedlander, M.D.

James Gusella, Ph.D.

Michael Hayden, M.D., Ph.D.

Steven Hersch, M.D., Ph.D.

Ron Kopito, Ph.D.

Marcy MacDonald, Ph.D.

Richard Morimoto, Ph.D.

Christopher Ross, M.D., Ph.D.

Leslie Thompson, Ph.D.

Erich Wanker, Ph.D.

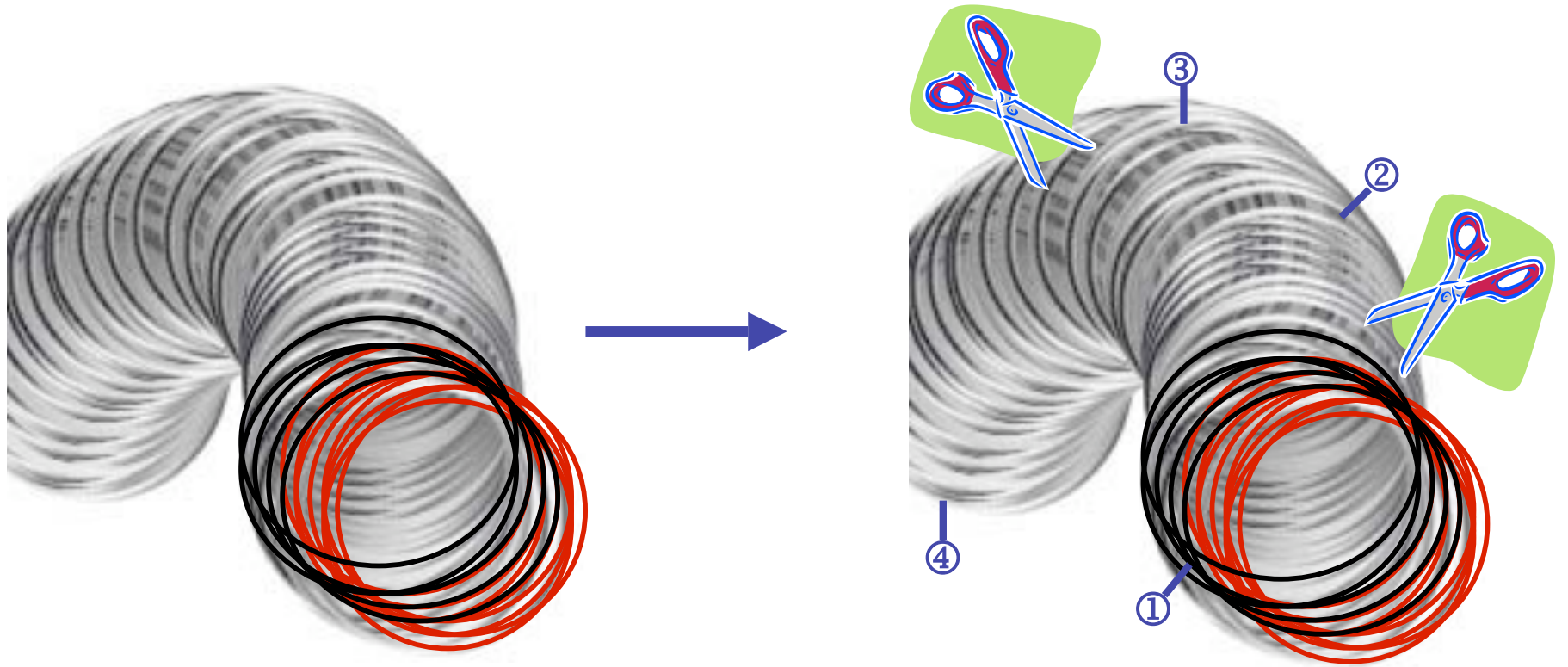
Huntingtin - a cargo barge



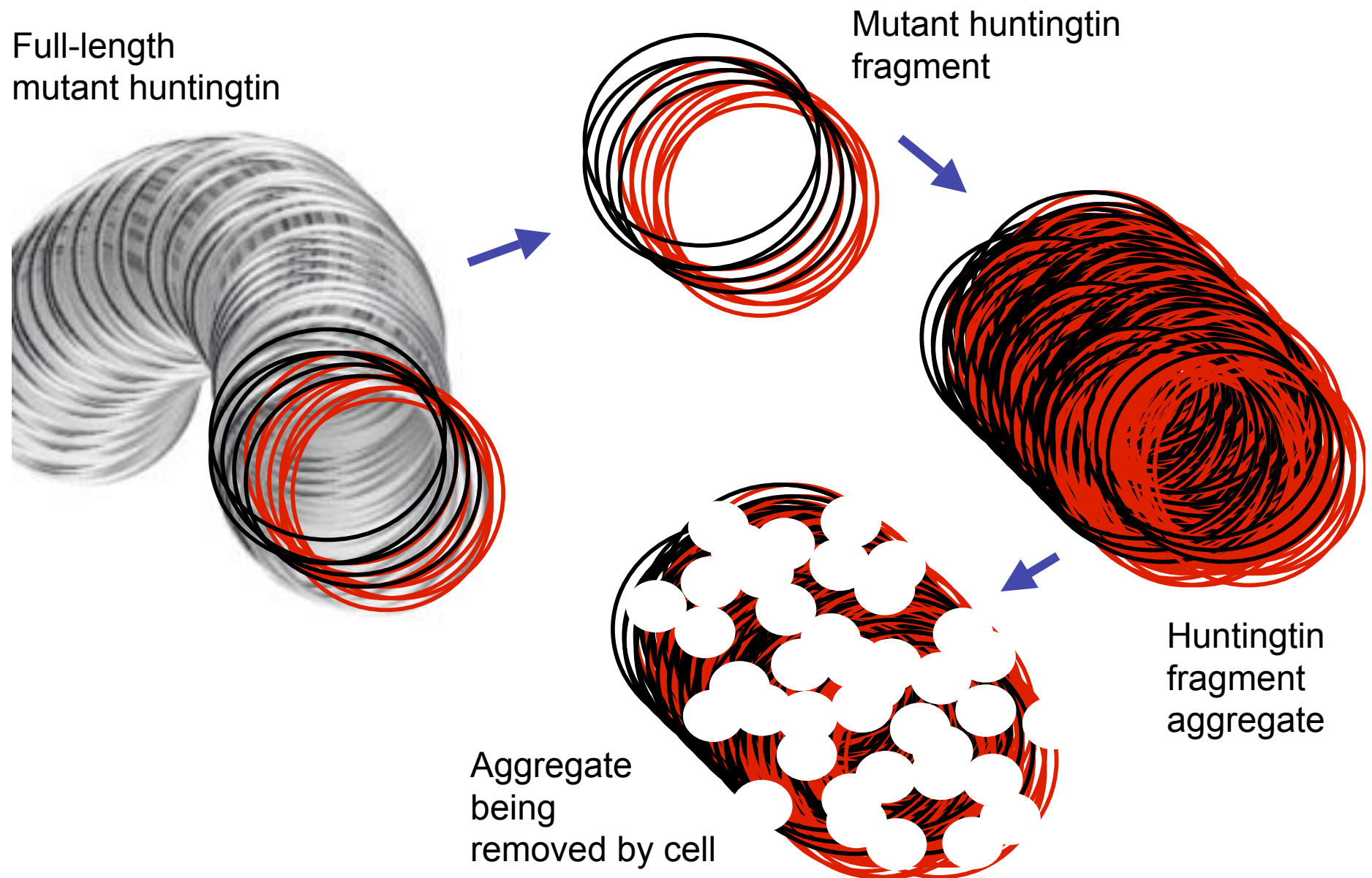
Huntingtin Function



Mitochondria & Energy Metabolism



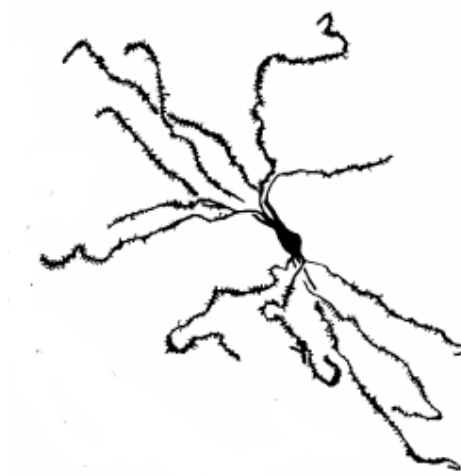
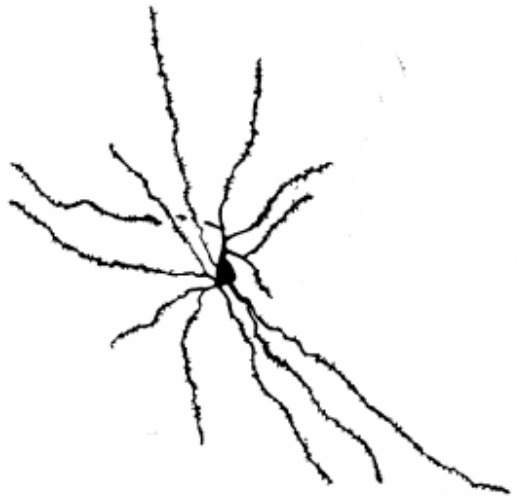
Huntingtin Proteolysis and Posttranslational Modification



Folding, Aggregation and Clearance of Mutant Huntingtin



Transcription

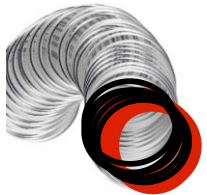


**Mutant
huntingtin**



Death

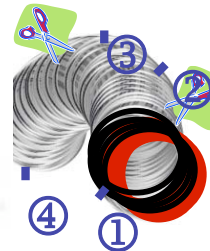
Lifeline of a brain cell with the HD mutation



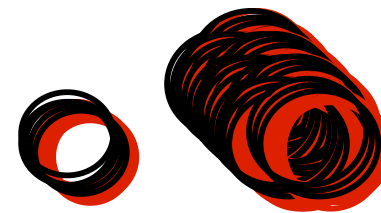
**Trigger
mechanism**



**Changes that
may disable
the brain cell**



**Changes related to
death of the
brain cell**





Michael Macor / The Chronicle





